

SEQUENCE LISTING

- <110> Sundelin, Johan Scarborough, Robert M.
- <120> Recombinant C140 Receptor, Its Agonists and Antagonists, and Nucleic Acids Encoding the Receptor
- <130> 44481-5006-09-US
- <140> US 10/643,627
- <141> 2003-08-19
- <150> US 10/127,691
- <151> 2002-04-23
- <150> US 08/097,938
- <151> 1993-07-26
- <150> US 08/390,301
- <151> 1995-01-25
- <150> US 08/474,414
- <151> 1995-06-07
- <160> 64
- <170> PatentIn Ver. 2.1
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- <212> DNA
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- <223> C140 receptor, genomic DNA and deduced protein sequences
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- acacaagaat tagacttcaa ccgtcaccaa ctgccctgtg taggacggtc ggtcactgaa 180
- agagaatatt gtctgcaata ctctaatgac atctgtctgt gttcatctga a atg ttc 237 Met Phe 1

cat tta aaa cac agc agc ctt act gtt gga cca ttt atc tca gta atg \$285\$ His Leu Lys His Ser Ser Leu Thr Val Gly Pro Phe Ile Ser Val Met \$5\$ 10 \$15\$

att ctg ctc cgc ttt ctt tgt aca gga cgc aac aac agt aaa gga aga 333 Ile Leu Leu Arg Phe Leu Cys Thr Gly Arg Asn Asn Ser Lys Gly Arg

25 30 20 agt ctt att ggc aga tta gaa acc cag cct cca atc act ggg aaa ggg Ser Leu Ile Gly Arg Leu Glu Thr Gln Pro Pro Ile Thr Gly Lys Gly 40 gtt ccg gta gaa cca ggc ttt tcc atc gat gag ttc tct gcg tcc atc 429 Val Pro Val Glu Pro Gly Phe Ser Ile Asp Glu Phe Ser Ala Ser Ile 477 ctc acc qqq aaq ctq acc acq gtc ttt ctt ccg gtc gtc tac att att Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro Val Val Tyr Ile Ile 75 qtg ttt qtg att ggt ttg ccc agt aat ggc atg gcc ctc tgg atc ttc 525 Val Phe Val Ile Gly Leu Pro Ser Asn Gly Met Ala Leu Trp Ile Phe 90 85 573 ctt ttc cga acg aag aaa cac ccc gcc gtg att tac atg gcc aac Leu Phe Arg Thr Lys Lys His Pro Ala Val Ile Tyr Met Ala Asn 100 105 ctg gcc ttg gcc gac ctc ctc tct gtc atc tgg ttc ccc ctg aag atc 621 Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp Phe Pro Leu Lys Ile 125 669 tcc tac cac cta cat ggc aac aac tgg gtc tac ggg gag gcc ctg tgc Ser Tyr His Leu His Gly Asn Asn Trp Val Tyr Gly Glu Ala Leu Cys 135 140 aag gtg ctc att ggc ttt ttc tat ggt aac atg tat tgc tcc atc ctc 717 Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn Met Tyr Cys Ser Ile Leu 155 150 765 ttc atg acc tgc ctc agc gtg cag agg tac tgg gtg atc gtg aac ccc Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp Val Ile Val Asn Pro 165 170 atg gga cac ccc agg aag aag gca aac atc gcc gtt ggc gtc tcc ttg 813 Met Gly His Pro Arg Lys Lys Ala Asn Ile Ala Val Gly Val Ser Leu 180 gca atc tgg ctc ctg att ttt ctg gtc acc atc cct ttg tat gtc atg 861 Ala Ile Trp Leu Leu Ile Phe Leu Val Thr Ile Pro Leu Tyr Val Met 200 210 195 aag cag acc atc tac att cca gca ttg aac atc acc acc tgt cac gat 909 Lys Gln Thr Ile Tyr Ile Pro Ala Leu Asn Ile Thr Thr Cys His Asp 215 220 gtg ctg cct gag gag gta ttg gtg ggg gac atg ttc aat tac ttc ctc 957 Val Leu Pro Glu Glu Val Leu Val Gly Asp Met Phe Asn Tyr Phe Leu 235 230

.4)

255

1005

tca ctq qcc att qqa qtc ttc ctq ttc ccq qcc ctc ctt act qca tct

Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala Leu Leu Thr Ala Ser

250

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cac tca gag aac aaa agg cag agg gct atc cga ctc atc acc gtg His Ser Glu Lys Lys Arg Gln Arg Ala Ile Arg Leu Ile Ile Thr Val 275 280 285 290	1101						
ctg gcc atg tac ttc atc tgc ttt gct cct agc aac ctt ctg ctc gta Leu Ala Met Tyr Phe Ile Cys Phe Ala Pro Ser Asn Leu Leu Val 295 300 305	1149						
gtg cat tat ttc cta atc aaa acc cag agg cag agc cac gtc tac gcc Val His Tyr Phe Leu Ile Lys Thr Gln Arg Gln Ser His Val Tyr Ala 310 315 320	1197						
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Gly Arg Ser Leu Ile Gly Arg Leu Glu Thr Gln Pro Pro Ile Thr Gly 35 40 45							
Lys Gly Val Pro Val Glu Pro Gly Phe Ser Ile Asp Glu Phe Ser Ala							

Ser Ile Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro Val Val Tyr Ile Ile Val Phe Val Ile Gly Leu Pro Ser Asn Gly Met Ala Leu Trp 90 Ile Phe Leu Phe Arg Thr Lys Lys His Pro Ala Val Ile Tyr Met 105 Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp Phe Pro Leu 120 Lys Ile Ser Tyr His Leu His Gly Asn Asn Trp Val Tyr Gly Glu Ala 130 Leu Cys Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn Met Tyr Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp Val Ile Val 170 Asn Pro Met Gly His Pro Arg Lys Lys Ala Asn Ile Ala Val Gly Val 185 Ser Leu Ala Ile Trp Leu Leu Ile Phe Leu Val Thr Ile Pro Leu Tyr 200 Val Met Lys Gln Thr Ile Tyr Ile Pro Ala Leu Asn Ile Thr Thr Cys 215 210 His Asp Val Leu Pro Glu Glu Val Leu Val Gly Asp Met Phe Asn Tyr 235 230 Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala Leu Leu Thr 250 Ala Ser Ala Tyr Val Leu Met Ile Lys Thr Leu Arg Ser Ser Ala Met Asp Glu His Ser Glu Lys Lys Arg Gln Arg Ala Ile Arg Leu Ile Ile Thr Val Leu Ala Met Tyr Phe Ile Cys Phe Ala Pro Ser Asn Leu Leu 300 Leu Val Val His Tyr Phe Leu Ile Lys Thr Gln Arg Gln Ser His Val 315 305 Tyr Ala Leu Tyr Leu Val Ala Leu Cys Leu Ser Thr Leu Asn Ser Cys 330 Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser Lys Asp Phe Arg Asp His 340 Ala Arg Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Asn Arg Met 360 355

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Gln Ile Ser Leu Ser Ser Asn Lys Phe Ser Arg Lys Ser Gly Ser Tyr

120

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					gtg Val											538
					atg Met											586
					ggg Gly											634
					ata Ile											682
					cag Gln 215											730
					ttg Leu											778
					ctg Leu											826
					tat Tyr											874
					tca Ser											922
					gcc Ala 295											970
					cat His											1018
					tac Tyr											1066
agc Ser	tgc Cys	atc Ile 340	gac Asp	ccc Pro	ttt Phe	gtc Val	tat Tyr 345	tac Tyr	ttt Phe	gtt Val	tca Ser	cat His 350	gat Asp	ttc Phe	agg Arg	1114
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Asp His Ala Lys Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Lys 355 360 cag atg caa gta tcc ctc acc tca aag aaa cac tcc agg aaa tcc agc Gln Met Gln Val Ser Leu Thr Ser Lys Lys His Ser Arg Lys Ser Ser 380 370 1255 tct tac tct tca agt tca acc act gtt aag acc tcc tat tgagtt Ser Tyr Ser Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr 390 <210> 4 <211> 398 <212> PRT <213> Homo sapiens Met Asn Val Leu Ser Phe Glu Gln Thr Ser Val Thr Ala Glu Thr Phe 10 Ile Ser Val Met Thr Leu Val Phe Leu Ser Cys Thr Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp Gly Thr Ser His Val Thr Gly Lys Gly Val Thr Val Glu Thr Val Phe Ser Val Asp Glu Phe Ser Ala Ser Val Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro 70 75 Ile Val Tyr Thr Ile Val Phe Val Val Gly Leu Pro Ser Asn Gly Met 90 Ala Leu Trp Val Phe Leu Phe Arg Thr Lys Lys Lys His Pro Ala Val 105 Ile Tyr Met Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp 115 Phe Pro Leu Lys Ile Ala Tyr His Ile His Gly Asn Asn Trp Ile Tyr 135 Gly Glu Ala Leu Cys Asn Val Leu Ile Gly Phe Phe Tyr Gly Asn Met 155 160 150 Tyr Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp 175 165 Val Ile Val Asn Pro Met Gly His Ser Arg Lys Lys Ala Asn Ile Ala Ile Gly Ile Ser Leu Ala Ile Trp Leu Leu Ile Leu Leu Val Thr Ile 205 200 195

Pro Leu Tyr Val Val Lys Gln Thr Ile Phe Ile Pro Ala Leu Asn Ile 210 215 220

Thr Thr Cys His Asp Val Leu Pro Glu Gln Leu Leu Val Gly Asp Met 225 230 235 240

Phe Asn Tyr Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala 245 250 255

Phe Leu Thr Ala Ser Ala Tyr Val Leu Met Ile Arg Met Leu Arg Ser 260 265 270

Ser Ala Met Asp Glu Asn Ser Glu Lys Lys Arg Lys Arg Ala Ile Lys 275 280 285

Leu Ile Val Thr Val Leu Ala Met Tyr Leu Ile Cys Phe Thr Pro Ser 290 295 300

Asn Leu Leu Val Val His Tyr Phe Leu Ile Lys Ser Gln Gly Gln 305 310 315 320

Ser His Val Tyr Ala Leu Tyr Ile Val Ala Leu Cys Leu Ser Thr Leu 325 330 335

Asn Ser Cys Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser His Asp Phe 340 345 350

Arg Asp His Ala Lys Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val 355 360 365

Lys Gln Met Gln Val Ser Leu Thr Ser Lys Lys His Ser Arg Lys Ser 370 380

Ser Ser Tyr Ser Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr 385 390 395

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<212> PRT

<213> Mus musculus

<220>

<223> Protein sequence of C140 receptor

<400> 5

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Val Met Ile Leu Leu Arg Phe Leu Cys Thr Gly Arg Asn Asn Ser Lys 20 25 30

Gly Arg Ser Leu Ile Gly Arg Leu Glu Thr Gln Pro Pro Ile Thr Gly

Lys Gly Val Pro Val Glu Pro Gly Phe Ser Ile Asp Glu Phe Ser Ala

50 55 60

Ser Ile Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro Val Val Tyr 70 Ile Ile Val Phe Val Ile Gly Leu Pro Ser Asn Gly Met Ala Leu Trp Ile Phe Leu Phe Arg Thr Lys Lys Lys His Pro Ala Val Ile Tyr Met 105 Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp Phe Pro Leu Lys Ile Ser Tyr His Leu His Gly Asn Asn Trp Val Tyr Gly Glu Ala Leu Cys Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn Met Tyr Cys Ser 160 155 145 Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp Val Ile Val 170 Asn Pro Met Gly His Pro Arg Lys Lys Ala Asn Ile Ala Val Gly Val 185 Ser Leu Ala Ile Trp Leu Leu Ile Phe Leu Val Thr Ile Pro Leu Tyr 195 Val Met Lys Gln Thr Ile Tyr Ile Pro Ala Leu Asn Ile Thr Thr Cys 215 His Asp Val Leu Pro Glu Glu Val Leu Val Gly Asp Met Phe Asn Tyr 230 235 240 Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala Leu Leu Thr 245 Ala Ser Ala Tyr Val Leu Met Ile Lys Thr Leu Arg Ser Ser Ala Met Asp Glu His Ser Glu Lys Lys Arg Gln Arg Ala Ile Arg Leu Ile Ile 275 Thr Val Leu Ala Met Tyr Phe Ile Cys Phe Ala Pro Ser Asn Leu Leu 295 Leu Val Val His Tyr Phe Leu Ile Lys Thr Gln Arg Gln Ser His Val 310 315 Tyr Ala Leu Tyr Leu Val Ala Leu Cys Leu Ser Thr Leu Asn Ser Cys 325 Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser Lys Asp Phe Arg Asp His 345 Ala Arg Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Asn Arg Met 355 360 365

Gln Ile Ser Leu Ser Ser Asn Lys Phe Ser Arg Lys Ser Gly Ser Tyr 370 375 380

Ser Ser Ser Ser Thr Ser Val Lys Thr Ser Tyr 385 390 395

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<211> 398

<212> PRT

<213> Homo sapiens

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Ile Ser Val Met Ile Leu Val Phe Leu Ser Cys Thr Gly Thr Asn Arg 20 25 30

Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp Gly Thr Ser His

Val Thr Gly Lys Gly Val Ile Val Glu Ile Val Phe Ser Val Asp Glu 50 55 60

Phe Ser Ala Ser Val Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro 65 70 75 80

Ile Val Tyr Ile Ile Val Phe Val Val Gly Leu Pro Ser Asn Gly Met 85 90 95

Ala Leu Trp Val Phe Leu Phe Arg Thr Lys Lys Lys His Pro Ala Val 100 105 110

Ile Tyr Met Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp
115 120 125

Phe Pro Leu Lys Ile Ala Tyr His Ile His Gly Asn Asn Trp Ile Tyr 130 135 140

Gly Glu Ala Leu Cys Asn Val Leu Ile Gly Phe Phe Tyr Gly Asn Met 145 150 155 160

Tyr Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp 165 170 175

Val Ile Val Asn Pro Met Gly His Ser Arg Lys Lys Ala Asn Ile Ala 180 185 190

Ile Gly Ile Ser Leu Ala Ile Trp Leu Leu Ile Leu Leu Val Thr Ile 195 200 205 Pro Leu Tyr Val Val Lys Gln Thr Ile Phe Ile Pro Ala Leu Asn Ile 210 215 220

Thr Thr Cys His Asp Val Leu Pro Glu Gln Leu Leu Val Gly Asp Met 225 230 235 240

Phe Asn Tyr Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala 245 250 255

Phe Leu Thr Ala Ser Ala Tyr Val Leu Met Ile Arg Met Leu Arg Ser 260 265 270

Ser Ala Met Asp Glu Asn Ser Glu Lys Lys Arg Lys Arg Ala Ile Lys 275 280 285

Leu Ile Val Thr Val Leu Ala Met Tyr Leu Ile Cys Phe Ile Pro Ser 290 295 300

Asn Leu Leu Val Val His Tyr Phe Leu Ile Lys Ser Gln Gly Gln 305 310 . 315 320

Ser His Val Tyr Ala Leu Tyr Ile Val Ala Leu Cys Leu Ser Thr Leu 325 330 335

Asn Ser Cys Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser His Asp Phe 340 345 350

Arg Asp His Ala Lys Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val 355 360 365

Lys Gln Met Gln Val Ser Leu Ile Ser Lys Lys His Ser Arg Lys Ser 370 380

Ser Ser Tyr Ser Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr 385 395

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<212> PRT

<213> Mus musculus

<220>

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Gly Phe Leu Leu Ser Ala Arg Thr Arg Ala Arg Arg Pro Glu Ser Lys 20 25 30

Ala Thr Asn Ala Thr Leu Asp Pro Arg Ser Phe Leu Leu Arg Asn Pro 35 40 45

Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Lys Asn Glu Ser 50 55 60

Gly Leu Thr Glu Tyr Arg Leu Val Ser Ile Asn Lys Ser Ser Pro Leu Gln Lys Gln Leu Pro Ala Phe Ile Ser Glu Asp Ala Ser Gly Tyr Leu 90 85 Thr Ser Ser Trp Leu Thr Leu Phe Val Pro Ser Val Tyr Thr Gly Val 105 100 Phe Val Val Ser Leu Pro Leu Asn Ile Met Ala Ile Val Val Phe Ile 120 Leu Lys Met Lys Val Lys Lys Pro Ala Val Val Tyr Met Leu His Leu 130 Ala Thr Ala Asp Val Leu Phe Val Ser Val Leu Pro Phe Lys Ile Ser 155 Tyr Tyr Phe Ser Gly Ser Asp Trp Gln Phe Gly Ser Glu Leu Cys Arg 170 Phe Val Thr Ala Ala Phe Tyr Cys Asn Met Tyr Ala Ser Ile Leu Leu 185 180 Met Thr Val Ile Ser Ile Asp Arg Phe Leu Ala Val Val Tyr Pro Met 205 200 -Gln Ser Leu Ser Trp Arg Thr Leu Gly Arg Ala Ser Phe Thr Cys Leu 220 210 215 Ala Ile Trp Ala Leu Ala Ile Ala Gly Val Val Pro Leu Val Leu Lys 235 Glu Gln Thr Ile Gln Val Pro Gly Leu Asn Ile Thr Thr Cys His Asp 250 245 Val Leu Asn Glu Thr Leu Leu Glu Gly Tyr Tyr Ala Tyr Tyr Phe Ser 260 Ala Phe Ser Ala Val Phe Phe Phe Val Pro Leu Ile Ile Ser Thr Val 280 Cys Tyr Val Ser Ile Ile Arg Cys Leu Ser Ser Ser Ala Val Ala Asn 295 300 Arg Ser Lys Lys Ser Arg Ala Leu Phe Leu Ser Ala Ala Val Phe Cys 305 310 Ile Phe Ile Ile Cys Phe Gly Pro Thr Asn Val Leu Leu Ile Ala His 330 Tyr Ser Phe Leu Ser His Thr Ser Thr Thr Glu Ala Ala Tyr Phe Ala Tyr Leu Leu Cys Val Cys Val Ser Ser Ile Ser Ser Cys Ile Asp Pro 365 360 355

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Leu Ile Tyr Tyr Tyr Ala Ser Ser Glu Cys Gln Arg Tyr Val Tyr Ser
                        375
Ile Leu Cys Cys Lys Glu Ser Ser Asp Pro Ser Ser Tyr Asn Ser Ser
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                                         395
385
Gly Gln Leu Met Ala Ser Lys Met Asp Thr Cys Ser Ser Asn Leu Asn
                405
Asn Ser Ile Tyr Lys Lys Leu Leu Thr
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<213> Mus musculus
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Arg Asn Asn Ser Lys Gly Arg
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Xaa Leu Leu Gly Lys
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Xaa Leu Ile Gly Arg
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<210> 11
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<212> PRT
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<222> (1)..(2)
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Xaa Xaa Leu Lys Gly
 1
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Xaa Xaa Ile Gly Arg
  1
<210> 13
<211> 6
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<210> 14
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Xaa Leu Ile Gly Arg Lys
<210> 15
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      antagonist
<220>
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Xaa Leu Ile Gly Arg Lys Glu Thr Gln Pro
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<210> 16
<211> 10
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<223> Description of Artificial Sequence: C140 receptor
      antagonist
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Xaa Leu Leu Gly Lys Lys Asp Gly Thr Ser
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\langle 223 \rangle Xaa at position 1 = (n-pentyl) 2-N-Leu
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Xaa Ile Gly Arg Lys
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      antagonist
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\langle 223 \rangle Xaa at position 1 = Me-N-(n-pentyl)
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Ile Ser Tyr His Leu His Gly Asn Asn Trp Val Tyr Gly Glu Ala Leu
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                                     10
Cys
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                                                          15
                  5
                                      10
Leu Pro Glu Glu Val Leu Val Gly Asp Met Phe Asn Tyr Phe Leu
                                  25
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His Tyr Phe Leu Ile Lys Thr Gln Arg Gln Ser His Val Tyr Ala
                                      10
                  5
<210> 23
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Ser Leu Ile Gly Arg Leu
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Ser Leu Ile Gly Ala Leu
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Ala Leu Ile Gly Arg Leu
<210> 30
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agonist

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agonist

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Pro Ile Thr Gly Lys Gly Val Pro Val Glu Pro Gly Phe Ser Ile Asp 50 55 60

Glu Phe Ser Ala Ser Ile Leu Thr Gly Lys Leu Thr Thr Val Phe Leu

Pro Val Val Tyr Ile Ile Val Phe Val Ile Gly Leu Pro Ser Asn Gly 85 90 95

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Met Ala Leu Trp Ile Phe Leu Phe Arg Thr Lys Lys Lys His Pro Ala 100 105 110

Val Ile Tyr Met Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile 115 120 125

Trp Phe Pro Leu Lys Ile Ser Tyr His Leu His Gly Asn Asn Trp Val 130 135 140

Tyr Gly Glu Ala Leu Cys Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn 145 150 155 160

Met Tyr Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr 165 170 175

Trp Val Ile Val Asn Pro Met Gly His Pro Arg Lys Lys Ala Asn Ile 180 185 190

Ala Val Gly Val Ser Leu Ala Ile Trp Leu Leu Ile Phe Leu Val Thr 195 200 205

Ile Pro Leu Tyr Val Met Lys Gln Thr Ile Tyr Ile Pro Ala Leu Asn 210 215 220

Ile Thr Thr Cys His Asp Val Leu Pro Glu Glu Val Leu Val Gly Asp 225 230 235 240

Met Phe Asn Tyr Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro 245 250 255

Ala Leu Leu Thr Ala Ser Ala Tyr Val Leu Met Ile Lys Thr Leu Arg 260 265 270

Ser Ser Ala Met Asp Glu His Ser Glu Lys Lys Arg Gln Arg Ala Ile 275 280 285

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Gln Ser His Val Tyr Ala Leu Tyr Leu Val Ala Leu Cys Leu Ser Thr 325 330 335

Leu Asn Ser Cys Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser Lys Asp 340 345 350

Phe Arg Asp His Ala Arg Asn Ala Leu Leu Cys Arg Ser Val Arg Thr 355 360 365

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1414

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Asn Asp Lys Tyr Glu Pro Glu Trp Glu Asp Glu Glu Lys Asn Glu Ser 50 55 60

Gly Leu Thr Glu Tyr Arg Leu Val Ser Ile Asn Lys Ser Ser Pro Leu Gln Lys Gln Leu Pro Ala Phe Ile Ser Glu Asp Ala Ser Gly Tyr Leu 90 95 Thr Ser Ser Trp Leu Thr Leu Phe Val Pro Ser Val Tyr Thr Gly Val 105 Phe Val Val Ser Leu Pro Leu Asn Ile Met Ala Ile Val Val Phe Ile 120 Leu Lys Met Lys Val Lys Lys Pro Ala Val Val Tyr Met Leu His Leu 130 Ala Thr Ala Asp Val Leu Phe Val Ser Val Leu Pro Phe Lys Ile Ser 150 155 Tyr Tyr Phe Ser Gly Ser Asp Trp Gln Phe Gly Ser Glu Leu Cys Arg 165 170 Phe Val Thr Ala Ala Phe Tyr Cys Asn Met Tyr Ala Ser Ile Leu Leu 185 180 Met Thr Val Ile Ser Ile Asp Arg Phe Leu Ala Val Val Tyr Pro Met 200 Gln Ser Leu Ser Trp Arg Thr Leu Gly Arg Ala Ser Phe Thr Cys Leu 210 215 Ala Ile Trp Ala Leu Ala Ile Ala Gly Val Val Pro Leu Val Leu Lys 235 225 Glu Gln Thr Ile Gln Val Pro Gly Leu Asn Ile Thr Thr Cys His Asp 250 245 Val Leu Asn Glu Thr Leu Leu Glu Gly Tyr Tyr Ala Tyr Tyr Phe Ser 260 Ala Phe Ser Ala Val Phe Phe Phe Val Pro Leu Ile Ile Ser Thr Val 280 Cys Tyr Val Ser Ile Ile Arg Cys Leu Ser Ser Ala Val Ala Asn 300 295 Arg Ser Lys Lys Ser Arg Ala Leu Phe Leu Ser Ala Ala Val Phe Cys 315 305 Ile Phe Ile Ile Cys Phe Gly Pro Thr Asn Val Leu Leu Ile Ala His 330 Tyr Ser Phe Leu Ser His Thr Ser Thr Thr Glu Ala Ala Tyr Phe Ala 340 Tyr Leu Leu Cys Val Cys Val Ser Ser Ile Ser Ser Cys Ile Asp Pro 365 355 360

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Leu Ile Tyr Tyr Tyr Ala Ser Ser Glu Cys Gln Arg Tyr Val Tyr Ser 370 380

Ile Leu Cys Cys Lys Glu Ser Ser Asp Pro Ser Ser Tyr Asn Ser Ser 385 390 395

Gly Gln Leu Met Ala Ser Lys Met Asp Thr Cys Ser Ser Asn Leu Asn 405 410 415

Asn Ser Ile Tyr Lys Lys Leu Leu Thr 420 425